

AMENDMENT TO THE CLAIMS:

Pursuant to the proposed revisions to 37 C.F.R. § 1.121, please amend the claims as follows. The following listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

~~1~~ 278. (Currently Amended) A method for evolving a polypeptide having an altered immunogenicity or stability, the polypeptide being encoded by a DNA substrate molecule, the method comprising:

- (a) providing a library of variants of the DNA substrate molecule;
- (b) transforming the variants of the DNA substrate molecule of (a) into host cells;
- (c) expressing the variants of (b) to provide polypeptide expression products and derivatizing the polypeptide expression products with a moiety capable of altering immunogenicity or stability; and
- (d) screening or selecting from the derivatized polypeptide expression products of (c) to identify at least one evolved polypeptide having an altered immunogenicity or stability relative to the polypeptide encoded by the DNA substrate molecule which polypeptide ~~that~~ is derivatized with the moiety.

~~2~~ 279. (Previously Presented) The method of claim ~~1~~ 278, wherein the variants of (a) are generated by one or more of: recursive sequence recombination, PCR mutagenesis, cassette mutagenesis, oligonucleotide-directed mutagenesis, site-directed mutagenesis, doped oligo mutagenesis, chemical mutagenesis, or propagation of the DNA substrate molecule through bacterial mutator strains.

~~3~~ 280. (Previously Presented) The method of claim ~~1~~ 278, further comprising:

- (e) recovering at least one evolved DNA substrate molecule encoding the at least one evolved polypeptide of (d); and
- (f) subjecting the at least one evolved DNA substrate molecule of (e) to mutagenesis to generate mutagenized products.

~~281.~~⁴ (Previously Presented) The method of claim ~~280~~³, wherein the mutagenesis comprises one or more of: recursive sequence recombination, PCR mutagenesis, cassette mutagenesis, oligonucleotide-directed mutagenesis, site-directed mutagenesis, doped oligo mutagenesis, chemical mutagenesis, or propagation of the DNA substrate molecule through bacterial mutator strains.

~~282.~~⁵ (Previously Presented) The method of claim ~~278~~¹, wherein the moiety capable of altering immunogenicity or stability is a polymer.

~~283.~~⁶ (Previously Presented) The method of claim ~~278~~¹, wherein the at least one evolved polypeptide has improved stability.

~~284.~~⁷ (Previously Presented) The method of claim ~~278~~¹, wherein the at least one evolved polypeptide has reduced immunogenicity.

~~285.~~⁸ (Previously Presented) The method of claim ~~278~~¹, wherein (c) comprises expressing the variants of (b) to provide polypeptide expression products, purifying the polypeptide expression products, and derivatizing the polypeptide expression products with a moiety capable of altering immunogenicity and/or stability.

~~286.~~⁹ (Previously Presented) The method of claim ~~278~~¹, wherein the derivatized polypeptide expression products of (c) are derivatized post-translationally.

~~287.~~¹⁰ (Previously Presented) The method of claim ~~278~~¹, wherein the at least one evolved polypeptide has reduced immunogenicity and improved stability.

~~288.~~¹¹ (Previously Presented) The method of claim ~~278~~¹, wherein the host cells comprise eukaryotic cells.

~~289.~~¹² (Previously Presented) The method of claim ~~280~~³, wherein the mutagenized products are used as the library of variants in a repeated (a).

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~~290.~~ (Previously Presented) A method for evolving a polypeptide having an altered immunogenicity, the polypeptide being encoded by a DNA substrate molecule, the method comprising:

- (a) providing a library of variants of the DNA substrate molecule;
- (b) transforming the variants of the DNA substrate molecule of (a) into host cells;
- (c) expressing the variants of (b) to provide polypeptide expression products;
- (d) screening or selecting from the polypeptide expression products of (c) to identify an evolved polypeptide having an altered immunogenicity relative to the polypeptide encoded by the DNA substrate molecule that is derivatized with the moiety;
- (e) recovering an evolved DNA substrate molecule that encodes the evolved polypeptide of (d); and
- (f) expressing the evolved DNA substrate molecule, thereby providing the evolved polypeptide having altered immunogenicity.

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~~291.~~ (Previously Presented) The method of claim 290, wherein the altered immunogenicity comprises reduced immunogenicity.

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~~292.~~ (Previously Presented) The method of claim 290, wherein the host cells comprise eukaryotic cells.

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~~293.~~ (Previously Presented) A method of identifying a polypeptide having an altered immunogenicity or stability, the method comprising:

- (a) providing a mixture of nucleic acid subsequences of two or more parental polynucleotides, wherein each parental polynucleotide differs from at least one other parental polynucleotide in at least one nucleotide and encodes at least one polypeptide or fragment thereof;
- (b) extending one or more of the nucleic acid subsequences with at least one polymerase to produce one or more recombined polynucleotides that each encode one or more polypeptide variants;

(c) expressing the one or more recombinated polynucleotides to provide the one or more polypeptide variants and derivatizing the one or more polypeptide variants with a moiety capable of altering immunogenicity or stability;

(d) screening or selecting the one or more polypeptide variants to identify at least one polypeptide variant having altered immunogenicity or stability compared to polypeptides derivatized with the moiety, which polypeptides are encoded by the two or more parental polynucleotides;

(e) recovering at least one recombinated polynucleotide encoding the at least one cytokine variant identified in step (d); and

(f) repeating (a)-(d) using the at least one recombinated polynucleotide recovered in step (e) as at least one of the two or more parental polynucleotides of a repeated step (a).

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~~294.~~ (Previously Presented) The method of claim ~~293~~¹⁶, wherein the host cells comprise eukaryotic cells.

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~~295.~~ (Previously Presented) A method for evolving a polypeptide having an altered immunogenicity or stability, the polypeptide being encoded by a DNA substrate molecule, the method comprising:

(a) providing a library of variants of the DNA substrate molecule;

(b) transforming the variants of the DNA substrate molecule of (a) into host cells;

(c) expressing the variants of (b) to provide polypeptide expression products and derivatizing the polypeptide expression products with a moiety capable of altering immunogenicity or stability; and

(d) screening or selecting from the derivatized polypeptide expression products of (c) to identify at least one evolved polypeptide having an altered affinity for a receptor or a ligand relative to the polypeptide encoded by the DNA substrate molecule which polypeptide is derivatized with the moiety.

¹⁹
~~296.~~ (Previously Presented) The method of claim ~~295~~¹⁸, wherein the host cells comprise eukaryotic cells.